Electroencephalography Improves the Prediction of Functional Outcome in the Acute Stage of Cerebral Ischemia

J.P.M. Cillessen, MD; A.C. van Huffelen, MD; L.J. Kappelle, MD; A. Algra, MD; J. van Gijn, MD, FRCPE

Background and Purpose We studied the value of clinical and electroencephalographic assessment in patients with acute first-ever supratentorial ischemia in predicting functional outcome after 1 year.

Methods In 55 consecutive patients admitted after a median interval of less than 24 hours, the degree of handicap was dichotomized as moderate (Rankin grade 1, 2, or 3) or severe (Rankin grade 4 or 5). Clinical deficits were categorized according to signs of a lacunar or a cortical syndrome. Without knowledge of clinical data, electroencephalograms (EEGs) were classified according to findings predicting good or poor prognosis. The outcome after 1 year was assessed as good (Rankin grade 3 or less) or poor (Rankin grade 4 or 5, or death) and was correlated to clinical data and to EEG findings in the acute stage.

Results Thirty patients with a moderate handicap on admission all had a good outcome (predictive value [PV] of the initial handicap, 1.00; 95% confidence interval [CI], 0.88 to 1.00). Of the 25 patients with severe handicap on admission a poor outcome occurred in 13 (PV, 0.52; 95% CI, 0.31 to 0.72). If these patients with severe handicap at baseline were subdivided according to clinical features, a lacunar syndrome predicted good outcome in 4 of 5 patients (PV, 0.80; 95% CI, 0.28 to 1.00), but a cortical syndrome predicted poor outcome in only 12 of 20 patients (PV, 0.60; 95% CI, 0.36 to 0.81). Of the 20 patients with severe handicap and a cortical syndrome at baseline, an EEG with features predicting a good prognosis correctly predicted good outcome in 6 of 7 patients (PV, 0.86; 95% CI, 0.42 to 1.00). An EEG with features predicting poor prognosis correctly predicted poor outcome in 11 of 13 patients (PV, 0.85; 95% CI, 0.55 to 0.98).

Conclusions Electroencephalography improves the prediction of functional outcome in patients with a severe neurological deficit in the acute stage of cerebral ischemia. This may have implications for the design of future intervention trials in acute stroke. 

Key Words • cerebral ischemia • electroencephalography • prognosis

In the acute stage of cerebral ischemia it may be difficult to predict whether patients with severe neurological deficit will recover or whether they will remain permanently disabled. Nevertheless, this is important not only for giving optimal support to the patients and their relatives but also as a guideline in the choice of intervention therapy, or at least as a factor for stratification in studies about acute stroke intervention therapy. The prognosis of cerebral infarction is determined mainly by the size of the lesion. Patients with a small deep infarct or a cortical infarct in a restricted area usually have a more favorable outcome than patients with a large cortical infarct. However, it is not always possible to reliably assess the subtype of an ischemic stroke in the acute stage; therefore, it may be difficult to predict functional outcome on the basis of clinical findings only.

The value of the electroencephalogram (EEG) and the quantitative EEG in cerebral ischemia in general has been studied extensively, and the prediction of outcome has been given special attention. The EEG has proved useful in distinguishing between small- and large-vessel ischemic strokes. There is no evidence that the EEG is superior to clinical assessment in the prediction of functional outcome, but the combination of clinical and EEG examination in the early stage of cerebral ischemia has never been studied.

We studied the predictive value of the EEG assessed by visual and computer analysis, both separately and in combination with the clinical findings, for functional outcome after 1 year.

Subjects and Methods

Patients who had been admitted to the University Hospital Utrecht, the Netherlands, for acute first-ever supratentorial ischemic stroke were included. Patients with previous brain disease that could interfere with clinical or EEG assessment were excluded. Two patients were excluded because of an infarct in the posterior fossa identified by computed tomographic (CT) scan.

Handicap was assessed according to the modified Rankin Scale on admission (days 0 through 7 after onset of ischemia, median interval less than 24 hours) and at 1 year. Patients were subdivided by clinical assessment (L.I.K.) into those with evidence of a lacunar syndrome (pure motor stroke, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis) and those with evidence of a cortical syndrome (combinations of ipsilateral motor or sensory deficit or both, with dysphasia, visuospatial disorder, or hemianopia). CT scan of the brain was obtained with a Philips Tomoscan LX between days 0 and 7 after onset of the ischemia (median,
day 0). In 31 patients a CT scan was performed a second time (days 2 through 26 after the onset of ischemia; median, day 7). Absence of any abnormality or the presence of a subcortical or a cortical infarct was assessed. Patients received the best available medical treatment or carotid endarterectomy as required.

EEG was performed with a 21-channel recorder between days 1 and 10 after onset of ischemia (median, day 3). The electrodes were placed according to the international 10-20 System. Both bipolar and common reference montages were used. A band width of 0.26 to 70 Hz (−3 dB) was used. Without knowledge of the clinical data the clinical neurophysiologist (A.C. van H.) interpreted the EEGs. The EEGs were classified as indicative of minor ischemia (good prognosis) or major ischemia (poor prognosis). Absence of any abnormality or the presence of only a slight asymmetry of the alpha or mu rhythm was considered a sign of minor ischemia and was thought to represent a lacunar infarct.13-12 Absence of diffuse slow activity with presence of some intermittent local (fronto-temporal) delta or theta activity was also considered a sign of minor ischemia and was thought to represent restricted cortical involvement.5-5-11 Unilateral presence of prominent, continuous, and polymorphic delta and theta activity on the same side, together with slowing of the frequency of the alpha or mu rhythm (more than 1 Hz) or depression of beta activity, or both, were considered signs of major ischemia representing a large cortical infarct.3,5-8-11 Each EEG was also quantitatively studied. Spectral analysis was applied to eight channels (F3-C3, F4-C4, P3-O1, P4-O2, F7-A1, F8-A2, T3, T4, T3-T4). In these channels EEG samples of 102.4 seconds were analyzed (20 epochs; epoch length, 5.12 seconds) with the Fast Fourier Transform. Left-right differences were studied by subtracting spectra from homologous derivations.7,8 Frequency differences of the alpha or mu rhythm, or both, of more than 0.4 Hz but less than 1.0 Hz were considered signs of minor ischemia. Frequency differences of the alpha or mu rhythm, or both, of more than 1.0 Hz or power density differences of more than 3 dB, or both, were considered signs of major ischemia.

All patients who were alive were reexamined 1 year after onset of stroke by one of us (J.P.M.C). Without knowledge of the findings on admission or the EEG data, the functional outcome was assessed as good if patients were still independent in most of their daily activities (Rankin grade 4 or 5) and as poor if patients needed daily or continuous help (Rankin grade 4 or 5). Patients who died from a stroke were also classified as having a poor outcome. To assess the outcome of patients who died from another cause we took the last grade before death.

Results

On admission, 30 patients had a Rankin grade of 1, 2, or 3, and 25 patients had a Rankin grade of 4 or 5. Ages ranged between 38 and 85 years (median, 64 years). Functional outcome after 1 year was good (Rankin grade 3 or less) in 42 patients and poor (Rankin grade 4 or 5 or death from stroke) in 13 patients (Table). Ten patients died in the first year, 1 as a result of a stroke and 9 from other causes. A Rankin grade of 1, 2, or 3 predicted good outcome in 30 of 30 patients (predictive value [PV], 1.00; 95% confidence interval [CI], 0.88 to 1.00), whereas a Rankin grade of 4 or 5 predicted poor outcome in only 13 of 25 patients (PV, 0.52; 95% CI, 0.31 to 0.72; Table). On admission, 17 patients showed a lacunar syndrome, and 38 patients showed a cortical syndrome. The presence of a lacunar syndrome predicted good outcome in 16 of 17 patients (PV, 0.94; 95% CI, 0.71 to 1.00), whereas the presence of a cortical syndrome predicted poor outcome in only 12 of 38 patients (PV, 0.32; 95% CI, 0.18 to 0.49; Table).

Prediction of Outcome in the Acute Stage by Means of Rankin Grade, Clinical Syndrome, and EEG Features in 55 Patients With First-Ever Supratentorial Ischemic Stroke

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Good (n=42)</th>
<th>Poor (n=13)</th>
<th>Predictive Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rankin grade 1, 2, 3</td>
<td>n=30</td>
<td>0</td>
<td>1.00*</td>
<td>(0.88-1.00)</td>
</tr>
<tr>
<td>Rankin grade 4, 5</td>
<td>n=12</td>
<td>13</td>
<td>0.52†</td>
<td>(0.31-0.72)</td>
</tr>
<tr>
<td>Lacunar syndrome</td>
<td>n=16</td>
<td>1</td>
<td>0.94*</td>
<td>(0.71-1.00)</td>
</tr>
<tr>
<td>Cortical syndrome</td>
<td>n=26</td>
<td>12</td>
<td>0.32†</td>
<td>(0.18-0.49)</td>
</tr>
<tr>
<td>EEG good prognosis</td>
<td>n=39</td>
<td>2</td>
<td>0.95*</td>
<td>(0.84-0.99)</td>
</tr>
<tr>
<td>EEG poor prognosis</td>
<td>n=6</td>
<td>11</td>
<td>0.79†</td>
<td>(0.49-0.95)</td>
</tr>
</tbody>
</table>

n indicates number of patients; 95% CI, 95% confidence interval.

*Good outcome; †poor outcome.

The first and second CT scans were normal in 4 patients. The CT scans showed a subcortical infarct in 22 patients and a cortical infarct in 29 patients. A subcortical infarct on the CT scans was present in 14 of 17 patients with a lacunar syndrome. A cortical infarct on the CT scans was present in 27 of 38 patients with a cortical syndrome.

Forty-one patients had an EEG with features indicating a good prognosis; in the other 14 patients the EEG predicted a poor prognosis. The EEG correctly predicted a good outcome in 39 of 41 patients (PV, 0.95; 95% CI, 0.84 to 0.99) and a poor outcome in 11 of 14 patients (PV, 0.79; 95% CI, 0.49 to 0.95; Table). The analysis of the EEG features, the functional outcome of patients, and the PV of EEGs in patients younger and in patients older than 65 years showed no statistically significant differences.

Fig 1 shows the flow chart of outcome assessed by the combined assessment using Rankin Scale, clinical syn-
drome, and EEG findings in all 55 patients. Five of the 25 patients with severe handicap at baseline had a lacunar syndrome, and 20 patients had a cortical syndrome. Outcome was good in 4 of 5 patients with a lacunar syndrome (PV, 0.80; 95% CI, 0.28 to 1.00) but poor in 12 of 20 patients with a cortical syndrome (PV, 0.60; 95% CI, 0.36 to 0.81; Fig 1). The EEG of the patient with severe handicap at baseline and a lacunar syndrome who had a poor outcome showed evidence of moderate cortical involvement. The EEGs of the 4 patients with a lacunar syndrome and a good outcome all showed features of a good prognosis.

In the 20 patients with severe handicap and a cortical syndrome at baseline, EEG assessment showed features of a good prognosis in 7 patients and of a poor prognosis in 13 patients (Figs 2 and 3). Outcome was good in 6 of the 7 patients with an EEG predicting good prognosis (PV, 0.86; 95% CI, 0.42 to 1.00) and poor in 11 of the 13 patients with an EEG predicting poor prognosis (PV, 0.85; 95% CI, 0.55 to 0.98; Fig 1). In 31 patients EEGs were repeated between days 11 and 24 (median day, 17); these were all classified in the same categories as the first EEGs.

In all patients the classification as minor or major ischemia was identical with that made by visual and quantitative analysis. Fifteen patients had a normal quantitative EEG. Twenty-six patients had a quantitative EEG showing features of minor ischemia. An asymmetry of less than 1.0 Hz of the peak frequency of the alpha rhythm was found in 14 patients, of the mu rhythm in 3 patients, and of both in 9 patients. The analysis of the quantitative EEG revealed asymmetry of the alpha rhythm (0.7 Hz) in only 1 patient in whom this was not detected on visual assessment. However, both visual and quantitative assessment led to the same classification of minor ischemia in this patient. Fourteen patients had a quantitative EEG with features indicating major ischemia; in all of those an asymmetry of the alpha peak frequency of more than 1.0 Hz and of the delta power density of more than 3 dB was found. In addition, a mu asymmetry of more than 1.0 Hz was present in 6 patients.

**Discussion**

Prediction of functional outcome in the early stage in patients with acute cerebral ischemia will be increasingly important with the advent of early intervention therapy; the effectiveness and safety of this therapy has to be evaluated in clinical trials. In the present study, a degree of handicap of 1, 2, or 3 on the modified Rankin Scale on admission was invariably associated with a good outcome, independently of the clinical syndrome. The few patients with severe handicap (Rankin grade 4 or 5) and a lacunar syndrome on admission also had a
favorable outcome after 1 year, with one exception. In contrast, we found it was very difficult to correctly predict functional outcome on clinical grounds in patients with a severe handicap and a cortical syndrome (PV, 0.60). In this particular group, in which early intervention might prevent severe disability, the diagnostic gain by means of the EEG was considerable (PV, 0.25; Fig 1).

Many previous studies have evaluated the prognostic value of EEG in cerebral ischemia. Our findings disagree with a recent review postulating that the EEG was not superior to clinical assessment. EEG can easily be performed in the first few hours after a stroke, and assessment as we presented here can be performed by the average well-trained electroencephalographer, since the differences between the two degrees of cerebral ischemia are simple and clear. EEG predictors of a good outcome are absence of slow activity together with no or only slight decrease in frequency of the alpha or mu rhythm or both. Superficial but limited ischemia, also predicting a good prognosis, causes intermittent theta and/or delta activity on the side of the infarction, accompanied by a slight asymmetry of background activity. EEG predictors of a poor outcome consist of prominent, continuous, and polymorphic delta activity together with slowing or depression of the alpha or beta activity, or both, in the ischemic hemisphere. The degree of depression of background activity correlates with functional outcome, as does the presence of delta activity.

Bamford et al showed that the distinction between lacunar and cortical syndromes is important regarding functional outcome. In our study this prediction was fairly accurate for lacunar syndromes but less reliable for cortical syndromes, probably because clinical assessment was performed in the first few days (usually on the first day). For this reason additional diagnostic tools have to supplement the clinical features in the acute stage, especially in patients with a severe handicap and a cortical syndrome. CT scanning is indispensable in the acute stage for exclusion of hemorrhagic lesions. EEG changes are present immediately after onset of ischemia, whereas CT scanning shows the extent of infarction only after 1 to 3 days. Magnetic resonance imaging scan also shows ischemia in the acute stage; however, this procedure is available in only a few centers, and even then it may be difficult to perform at short notice, particularly in the severely handicapped patients in whom prognostication is difficult. In this study not all EEGs were performed on the first day, but this could only have affected our results adversely because the earlier the EEG is recorded, the better the EEG changes caused by ischemia can be assessed.

Quantitative EEG analysis only confirmed the visually analyzed EEGs in our study; therefore, it is not neces-
sary for the prediction of functional outcome in the acute stage of cerebral ischemia.
To summarize, EEG improves the prediction of functional outcome in patients with a severe handicap (Rankin grade 4 or 5) in the acute stage of cerebral ischemia. In patients with a moderate handicap at admission, EEG has no additional PV. This prognostic information may be relevant for patients in whom early intervention therapy is considered.

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References
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